

A Hospital Based Research to Evaluate the Incidence and Severity of Vitamin D Insufficiency in type 2 Diabetes Patients

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Abstract

Aim: The aim of the study to assess the prevalence and severity of vitamin D deficiency in type 2 DM. **Methods:** The present study was conducted in the Department of General Medicine, Madhubani Medical College and Hospital, Madhubani, Bihar, India, from January 2020 to June 2020. Total 180 participants were including in the study out of which 90 healthy people were include as case (Group A) and 90 type 2 diabetic patients as controls (Group B). Routine laboratory Investigations like CBC, FBS, RBS, PP2BS, HbA1C, blood urea, serum creatinine, lipid profile, urine albumin and Vitamin D3 levels were done by standard methods in central laboratory of Institute. **Results:** Frequency Distribution of Participants according to Severity of Vitamin D level noted. Prevalence of low vitamin D level in healthy population was only 22.22% in my study, while prevalence was 85.56 % in Diabetic group. Among diabetic patients having abnormal Vitamin D level, majority (68.59%) were having insufficiency, only 16.67% were having overt vitamin D deficiency in Diabetic patients. In patients with controlled diabetes as per HbA1C criteria, the prevalence of sufficient, Insufficient and Deficient Vitamin D was 20%, 67.5% and 12.5% respectively, where in patients with uncontrolled diabetes it was 8%, 74% and 18% respectively. More number of diabetic patients with uncontrolled status (18%) was having overt vitamin D deficiency in comparison to controlled status (12.5%). There is a significant association between the maintenance of euglycemia and severity of Vitamin D level in diabetic patients, as the p value is less than 0.05. **Conclusion:** We concluded that the control of diabetic status is mandatory in order to prevent vitamin D deficiency.

Keywords: Serum vitamin D level, Type 2 diabetes mellitus, Vitamin D deficiency.

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Introduction

Vitamin D is a pleiotropic hormone known to play an immunomodulatory role in addition to Calcium and bone

metabolism.[1,2] Receptors for its activated form have been identified on pancreatic β cells and immune cells.[3,4] Studies have

proven association of vitamin D deficiency with viral and bacterial infection. Foot infection accounts for 20% of hospitalization of diabetic patients annually.[5,6] Pathogenesis of diabetic foot and subsequent infections is related to immunological defects along with neuropathy and vascular abnormalities being the major contributors.[7]

Different studies have shown that deficiency of vitamin D leads to immune cell dysfunction, β cell damage and impaired insulin production.[3,8] In addition to hyperglycaemia, vitamin D deficiency could also be linked to an altered immune system of patients with diabetes, rendering them susceptible to foot infection and unfavourable prognosis. Vascular calcification, long thought to be result of passive degeneration, involves a complex, regulated process of bio mineralization resembling osteogenesis. Vascular calcification is an important development in progression of vasculopathy. Diabetes mellitus contributes significantly to high prevalence of peripheral vascular disease and lower extremity amputation in these subjects. Vascular calcification is also associated with other manifestation of cardiovascular diseases like hypertension, coronary insufficiency and increased mortality in patients with diabetes mellitus.

Traditionally, medial arterial calcification has been associated with ageing, advanced chronic kidney disease and long-standing diabetes mellitus with diabetic neuropathy. Factors that potentiate medial arterial calcification in diabetes mellitus may include metabolic and hormonal along with activation of receptor activator of nuclear factor Kappa B ligand/osteoprotegerin (RANK-L/OPG) signalling pathway.⁶ Interleukins, 25(OH) vitamin D, sex, parathyroid hormone (PTH), lipoprotein, steroids, thyroid etc. directly or indirectly regulate RANK-L/OPG pathway.[7]

The literature on the role of 25(OH) vitamin D in vascular calcification is ambiguous. Experimentally higher 25(OH) vitamin D

level have been associated with increased vascular calcification while *in vivo*, lower level of 25(OH) vitamin D seems to have this effect. This suggests that 25 (OH) vitamin D may have a biphasic relation with risk promoting Vascular Calcification in both excess and deficiency.[8]

Material and Methods

The present study was conducted in the Department of General Medicine, Madhubani Medical College and Hospital, Madhubani, Bihar, India, from January 2020 to June 2020, after taking the approval of the protocol review committee and institutional ethics committee.

Methodology

The technique, risks, benefits, results and associated complications of the procedure were discussed with all patients. Total 180 participants were including in the study out of which 90 healthy people were include as case (Group A) and 90 type 2 diabetic patients as controls (Group B). Controls include age and sex matched healthy individuals. Patients with chronic kidney disease, patients taking calcium supplements or vitamin D supplements within last 3 months, patients suffering from any known chronic illness were excluded from this study. Routine laboratory Investigations like CBC, FBS, RBS, PP2BS, HbA1C, blood urea, serum creatinine, lipid profile, urine albumin and Vitamin D3 levels were done by standard methods in central laboratory of Institute. The value of serum vitamin D level was further divided in following category: sufficient = 30-100ng/ml, insufficient=20-29ng/ml, deficiency = less than 20ng/ml.

Statistical Methods

Results

In the study population, the mean age of group A (case) was 49.18 ± 9.88 years while that of group B (control) was 47.82 ± 9.76 years. Total 95 males and 85 females were enrolled in study. 66.67% of group A were male and 33.33% female. Group B (control)

had 45% males and 55% female. On evaluation of investigation profile of both group A and group B, mean values of haematological parameters in form of haemoglobin, total count and platelet were within normal limit and comparable in both groups. Surprisingly mean value of renal function test parameters, blood urea and serum creatinine were within normal range for diabetic group also, though 10% of patients had abnormal serum creatinine value and it range from 2.43 to 4.4 mg/dl.

Mean value of all lipid profile component were in normal limit in both the group, but

38.89% of diabetic patients had dyslipidaemia and commonest dyslipidaemia was hyper-triglyceridemia in 27% patients. Frequency Distribution of Participants according to Severity of Vitamin D level noted. Prevalence of low vitamin D level in healthy population was only 22.22% in my study, while prevalence was 85.56 % in Diabetic group. Among diabetic patients having abnormal Vitamin D level, majority (68.59%) were having insufficiency, only 16.67% were having overt vitamin D deficiency in Diabetic patients (table 1.)

Table 1: Severity grading of vitamin d deficiency in cases and controls

	Case =90	%	Control=90	%
Deficiency	15	16.67	nil	-
Insufficient	62	68.89	20	22.22
Sufficient	13	14.44	70	7.78

Table 2: The association of severity of vitamin D level with the category of diabetes control

Diabetes control	Vitamin D Level			p value
	Sufficient	Insufficient	Deficiency	
Controlled Diabetic (N = 40)	8(20%)	27 (67.5%)	5(12.5%)	2.98
Uncontrolled Diabetic (N= 50)	4(8%)	37 (74%)	9 (18%)	0.004*

Test applied: Chi-square test

In patients with controlled diabetes as per HbA1C criteria, the prevalence of sufficient, Insufficient and Deficient Vitamin D was 20%, 67.5% and 12.5% respectively, where in patients with uncontrolled diabetes it was 8%, 74% and 18% respectively. More number of diabetic patients with uncontrolled status (18%) was having overt vitamin D deficiency in comparison to controlled status (12.5%). There is a significant association between the maintenance of euglycemia and severity of Vitamin D level in diabetic patients, as the p value is less than 0.05 (Table 2).

Pearson correlation test showed negative correlation between HbA1C level and mean vitamin D level in Diabetic group as $r = -0.251$, $p \text{ value} = <0.001$. It suggests as HbA1c level increase, the level of vitamin

D decreases, so more severe the hyperglycaemia and poorer the control of diabetes status, there was more severe the vitamin D deficiency.

We also compare the mean value of vitamin D deficiency with the duration of Diabetes, but there was no significant relation between duration of diabetes and serum vitamin D deficiency ($P \text{ value} >0.5$).

Diabetic nephropathy was the most common micro vascular complication seen in type 2 diabetic patients. it was found that all three important microvascular complications: - diabetic retinopathy, diabetic nephropathy and peripheral neuropathy did not have any significant correlation with serum Vitamin D level as p value is greater than 0.05 for all three parameters (Table 3).

Table 3: Comparison of mean vitamin D level with duration and micro vascular complication of diabetes mellitus

	Parameters		Mean value of vitamin D (ng/dl)	p value
Duration of diabetes	0-5 years		27.31±6.83	0.240
	5-10 years		29.5±5.87	
	>10 years		26.84±3.97	
Micro-vascular complication	Diabetic retinopathy	Present	24.83±5.331	0.069
		Absent	28.17±5.94	
	Diabetic nephropathy	Present	30.33±5.83	0.057
		Absent	27.86±6.89	
	Peripheral neuropathy	Present	26.39±4.87	0.120
		Absent	29.46±5.99	

Test applied: One-way ANOVA. t-test

Hypertension was most common co-morbidity found in diabetic group (16.67%) followed by ischemic heart disease (5.55%). Serum vitamin D level was measured in all participants. 85.56 of diabetic population was having less than normal vitamin D level, while only 22.22% had less than normal vitamin D level in group B(control). Mean value of vitamin D in type 2 Diabetic patients was 28.93±6.87 ng/dl and mean value of vitamin D in healthy individuals was 37.31±4.99 ng/dl.

Table 4: Subgroup analysis- mean vitamin D level in diabetes patients in relation with age, gender and associated co-morbidities

Parameters (Number of patients)		Mean value of vitamin D	p value
Age group	Below 35 (75)	27.42±5.85	0.230
	Above 35 (15)	27.12±3.69	
Gender	Male (62)	30.25±5.46	0.022*
	Female (28)	27.22±4.58	
HTN	Yes (15)	23.56±4.92	0.031*
	No (75)	27.48±6.61	
IHD	Yes (5)	30.33±4.62	0.130
	No (85)	28.37±5.72	

test applied: t-test

Discussion

However, the prevalence of vitamin D deficiency in India is around 50-90% in normal healthy population.[9] In our study, prevalence of vitamin D deficiency is 22.22% in normal population which is similar to worldwide prevalence but very less in comparison to prevalence shown in Indian studies. This low prevalence in healthy population was contradictory to other Indian studies. Another on-going study on vitamin D level done in similar region had also showed 16% prevalence of

vitamin D deficiency in healthy population. Vitamin D exerts its effect on calcium metabolism and hence affects skeletal system; however, it also has extra skeletal effects like that on cardiovascular system, endocrine disorders and autoimmune disorder. Several reports have ascribed an active role to vitamin D in the functional regulation of the endocrine pancreas, particularly the beta-cells.

India is already declared as 'Capital of Diabetes'. Diabetes mellitus is accepted as major emerging epidemic in India, as India

is having 41 million of diabetic patients currently and it will go up to 70 million by year 2025. As vitamin D has been showed to have effect on pathophysiology of diabetes and have very high prevalence of vitamin D deficiency, so we have taken up this study to see effect of both high prevalence diseases on each other.

Various studies done in different geographical region and cultural background have shown varied range of prevalence of vitamin D deficiency in diabetic group ranging from 67%-98.8%.[8-11] Our study along with Bashir et al and Ifigenia-Kostoglou A et al studies had shown higher prevalence of vitamin D deficiency in diabetes mellitus patients compared to healthy individuals, but two other studies had shown no difference of prevalence between diabetic and healthy population.[9-12] So, we have compared the mean value of serum vitamin D level in diabetic patients and in healthy population of various study. Various studies including our study had low mean level of vitamin D for diabetic patients in comparison to healthy population.[9,12,13]

In patients with controlled diabetes as per HbA1C criteria, the prevalence of sufficient, Insufficient and Deficient Vitamin D was 20%, 67.5% and 12.5% respectively, where in patients with uncontrolled diabetes it was 8%, 74% and 18% respectively. More number of diabetic patients with uncontrolled status (18%) was having overt vitamin D deficiency in comparison to controlled status (12.5%). There is a significant association between the maintenance of euglycemia and severity of Vitamin D level in diabetic patients, as the p value is less than 0.05. Similar results was shown by Mukherjee B et al. Mean level of vitamin D is low in uncontrolled diabetic patients (19.47 ± 4.76) as compared to controlled diabetic patients (23.63 ± 3.71).[13] Modi KD et al found that vitamin D levels in patients with controlled diabetes was 22.4 ± 18.6 while in uncontrolled diabetic patients it was lower,

19.9 ± 18.3 which is statistically significant.[14] Overall insufficiency is more common than deficiency state in diabetic patients regardless of diabetic control status, but severe vitamin D deficiency is more prevalent when patients were having uncontrolled diabetes than controlled diabetes (18% and 12.5% respectively). On Pearson correlation, the study has demonstrated negative correlation between HbA1C level and serum vitamin D level. It suggests that as HbA1C level increase, there is decrease in serum vitamin D level. Ifigenia-Kostoglou A et al had also found that 25(OH) D3 levels were inversely associated with HbA1c when the patient and control groups were analysed together ($p = 0.008$, $r^2 = 0.058$, linear regression analysis).[12] Study by Mukherjee B et al also indicates there is a definite negative correlation between Vitamin D levels and diabetes ($r = -0.94$ and -0.97) and poorly controlled diabetics have further lower values of Vitamin D.[13] A study by Akshay kumar SV et al showed a negative negligible correlation between vitamin D levels and HbA1C, which was not statistically significant ($r = 0.017$, p value 0.741).[11] The inverse relationship between vitamin D level and glycaemic control in this study support an active role of vitamin D in pathogenesis of type 2 diabetes mellitus.

Duration of diabetes and presence of microvascular complication do not have effect on serum vitamin D level. No effect of increasing age was observed on vitamin D status in diabetic patients, and we could not able to find such association in other studies. Female diabetic patients were having lower vitamin D level compared to male counterparts; the reason might be less exposure to sun due to household activity. Hypertension was the most common comorbidity found in diabetic patients (16.67%) in our study. Study by Shalini P et al found that Vitamin D deficiency is more prevalent (80.4%) in hypertensive patients than healthy (67.7%) individuals.[15]

Conclusion

The most active vitamin D metabolite, 1,25-dihydroxyvitamin D₃, induces antimicrobial peptides production in keratinocytes from diabetic foot ulcers. This study opens up an issue of recognizing vitamin D deficiency as a possible risk factor for diabetic foot infections and suggests the need for vitamin D supplementation in such patients to prevent or to adjuvant the antibiotic therapy for control of infection. Our data also raise the possibility that 25(OH)D might provide an adjunctive method for early detection of risk for foot complications in diabetes.

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